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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,152	02/17/2004	Andreas Hefel	RBL0109	1277

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EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/780,152	HEFEL, ANDREAS	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,23,24,26,28,29,32,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23,24,26,28,29,32,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/13/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of Applicant's Arguments/Remarks, amended claims, **RCE** and IDS filed on 09/13/10 is acknowledged.

Claims 1-20, 22, 25, 27, 30-31 and 33 have been cancelled in this Application.

Claims 21 has been amended.

Accordingly, claims **21, 23-24, 26, 28-29, 32 and 34-35** are under prosecution.

The rejections not reiterated herein have been withdrawn in light of claims amendments.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 21, 23-24, 26, 28-29, 32 and 34-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Instant claim 21 recites the limitation first active and the second active which makes the claim indefinite because it is not clear if applicant intends to claim same active ingredient or two different active ingredients. Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 21, 23-24, 26, 28-29, 32 and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata (EP 835654 A1 of record) in view of Walter (GB 2257358 A, presented in IDS) or vice versa.

Shibata teaches a method of producing a pharmaceutical preparation with sustained effect for oral administration of a pharmacologically active ingredient, the method comprising admixing a predetermined amount of said pharmacologically active ingredient with a predetermined amount of glucomannan (claim 4). The reference discloses that glucomannan makes a very viscous solution when dissolved in water and that glucomannan is not decomposed in the small intestine but is decomposed in the large intestine by Escherichia coli and loses its viscosity. The reference discloses the possibility of properly delaying absorption of a drug in the small intestine both by suppressing conveyance of the drug though the small intestine in the direction to the anus and suppressing diffusion of the drug in the solution (thus active substance is released in delayed release manner), both making use of the viscosity of the solution. As a result, the inventor has found that when glucomannan is orally administered

together with a drug, gradual absorption of the drug occurred over a prolonged time period (thus increase of the nutrient-bio-availability of vital substances) compared with the case without administration of glucomannan, and that there is no reduction of overall absorption of the drug (thus separated from each other in their function) (page 2, lines 28-38). Thus, the present invention provides a pharmaceutical preparation with sustained effect for oral administration of a pharmacologically active ingredient comprising a mixture of said pharmacologically active ingredient and glucomannan (thus the embedded active substances are slowly released for resorption). In accordance with the present invention, the length of time during which the absorption of the pharmacologically active ingredient takes place may be conveniently controlled by simply adjusting the proportion of glucomannan to the amount of the active ingredient. Thus, the present invention allows sustainment of pharmacological effect of a variety of active ingredients orally administered to mammals including human (page 2, lines 38-44). Shibata further teaches the pharmaceutical preparation may be in any convenient form suitable to oral administration, such as a powder, granules, capsules, tablets, an aqueous preparation (page 3, lines 20-22).

It is to be noted that claims 26 and 28 provide the functional limitations once the active substance is introduced into human or animal, since the claimed compound is similar to the compound disclosed in the prior art, the functional limitations are considered to be associated with process.

The reference discloses that it is possible to combine two or more active ingredients with similar or different activities, see page 3, lines 18-20. The preparation

also includes gel type preparation, it may be possible to add excipients and coloring material and binders for granules, see page 3, lines 20-25. Regarding the limitations the active substance is bound within the interstices of the lattice structure, it is the position of the examiner that since same glucomannan is taught in prior art and introduction of active substance is also taught in prior art, the positioning of active substance in lattice structure will be same as claimed.

The teachings of Shibata have been discussed above. Shibata suggests making granules of the composition but does not teach the process of making the composition.

Shibata does not specifically disclose providing first and second composition, although the reference suggests that more than one active can be included in the composition.

Walter discloses a composition comprising vitamins, enzymes, coenzymes, minerals, trace elements and/or microorganisms that are embedded, separately with regard to function in carrier substances with formation of protective films against harmful effects so that, with sufficient moisture absorption, **in vivo and in vitro biocatalytic processes can be initiated and controlled**. Suitable protective substances are preferably sodium salts and potassium salts of silicic acid and nonionic polysaccharides, in particular from the family consisting of the galactomannans (page 2, Paragraph 2 and **claim 5**).

The process of mixing and drying is depicted on page 4, paragraph 4, page 7, paragraph 1 and example 2). It is further disclosed that the **granulation** can be influenced by the spraying rate and the enzyme powders are

obtained in a relatively **narrow particle size ranges** after drying (page 8, paragraph 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the process of making a composition comprising active ingredient embedded in glucomannan which are functionally separated from each other as taught by Walter in the teachings of Shibata because Walter teaches that such composition helps in controlled biocatalytic processes. One of ordinary skill would have been motivated to do so because Shibata teaches oral administration of composition comprising active ingredient in glucomannan for controlled and gradual absorption of the drug over a prolonged time period and Walter teaches process of making such composition comprising active ingredient embedded in glucomannan.

It would have been obvious to one of ordinary skill in the art at the time of instant invention to formulate two compositions independently comprising similar or different active ingredients embedded in glucomannan as taught by Walter because Walter teaches that such preparation provides functionally separated compositions with controlled in-vivo bioactive processes once administered. Since Shibata suggests including one or more active preparations in glucomannan and Walter teaches method of making such preparation, one of ordinary skilled in the art would have had reasonable expectation of success in preparing and administering to humans, first and second active agents functionally separated due to glucomannan with no antagonistic interactions.

6. Claims 21, 23-24, 26, 28-29, 32 and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baichwal (WO 97/26865) of record.

Baichwal teaches a sustained-release formulation for use in oral solid dosage forms includes from about 10 to about 40 percent or more by weight galactomannan gum; from about 1 to about 20 percent by weight of an ionizable gel strength enhancing agent and an inert pharmaceutical filter (see Abstract). Baichwal also teaches in certain preferred embodiments for the invention, the sustained release matrix further comprises a hydrophobic material in an amount effective to slow the hydration of the gum without disrupting the hydrophilic matrix formed by the homolysaccharide when the formulation is exposed to fluids in an environment of use. This may be accomplished by **granulating** the sustained release matrix prior to the incorporation for the medicament. The hydrophobic material may be selected from alkylcelluloses, acrylic and/or methacrylic acid polymers or copolymers, hydrophobic vegetable oils, zein, as well as other pharmaceutically acceptable hydrophobic materials known to those skilled in the art (page 9, lines 9-22). Baichwal also teaches the homopolysaccharide gums used in the present invention include the **galactomannan**, i.e. polysaccharides which are composed solely of mannose and glactose. Galactomannans which have higher proportions of unsubstituted mannose are preferred in certain embodiments. Locust bean gum, which has a higher ratio of mannose to the galactose, is especially preferred as compared to other galactomannans such as guar and hydroxyproply guar (page 6, lines 13-18). Baichwal further teaches accordingly, the ingredients of the sustained

release pharmaceutical excipient prepared in accordance with the present invention may be subjected to wet granulation before the medicament is added. In this technique, the desired amounts of the homopolysaccharide, the ionizable gel strength enhancing agent, and the inert filler are mixed together and thereafter a moistening agent such as water, propylene glycol, glycerol, alcohol or the like is added to prepare a moistened mass. Next, the moistened mass is dried. The dried mass is then milled with conventional equipment product is ready to use. The granulate thus obtained has certain advantages including the fact that it is free-flowing, has good cohensive properties, and can be admixed with an active agent (e.g., drug) and can be directly compressed into tablets (page 11, lines 7-23). Baichwal teaches alternatively, **the medicament may be wet-granulated** in appropriate circumstance with one or more of the ingredients of the sustained release excipient. The remaining release excipient ingredients can simply be **admixed** to the resultant pre-granulated material or granulated together with the pre-granulated ingredients in a second wet granulation step (page 12, lines 3-9). Baichwal further teaches finally, in further alternative embodiments of the invention, a therapeutically active agent can be incorporated (admixed, granulated, etc.) with any of the ingredients of the sustained release excepient, if so desired (page 13, lines 24-30). Baichwal at last teaches examples of such therapeutically active agents include hormones (e.g., insulin, heparin), **vitamins etc**. (page 16, last paragraph bridging page 17).

The reference teaches dry blending and also wet granulating the mixture and then admixing the active ingredient, see page 5, lines 10-15. The active ingredient can

be admixed or granulated with any of the sustained release ingredients, see page 13, and lines 25-27. The average particle size of granulated excipient ranges from 50 microns to about 400 microns and preferable from 185 microns to 265 microns, page 15, lines 18-22. Various active ingredients that can be included are on page 16, lines 14-28.

It would have been obvious to one of ordinary skill in the art at the time of instant invention to formulate two compositions independently comprising similar or different active ingredients embedded in glucomannan/galactomannan as taught by Baichwal because Baichwal teaches that medicament may be wet-granulated in appropriate circumstance with one or more of the ingredients of the sustained release excipient and also teaches the method of making granules comprising galactomannan wherein active ingredient can be admixed or granulated. Since Baichwal teaches making granules for oral administration, it would have been obvious to one of ordinary skill to have utilized different active ingredients in making granules and administering such granules orally. Since the active ingredients will be embedded or mixed within galactomannan one of ordinary would expect no antagonism between the two granular particles once administered to human beings. Since the process of making the granular particle comprising galactomannan is substantially similar to the prior art, one would expect the formation of an aqueous envelope in animals digestive part.

Response to Arguments

7. Applicant's arguments filed 09/13/10 have been fully considered but they are not persuasive.

Applicant argues that the office continues to reject the pending claims under a combination of Shibata and Walter. Applicant believes that the amendments currently made to Claim 21, more clearly differentiates the claimed invention from the combination of Shibata and Walter. Applicant asserts that Walter teaches preventing a combination of acting ingredients from interacting with other constituents of a digestive tract when they are embedded in different matrixes not when they are embedded in the same matrix.

Applicant's arguments are not persuasive because while it is true that Walter does not exemplify incorporating different actives in different matrixes, however, Walter does teach the process of introducing the known actives in the known galactomannan in a granular formulation. Walter also teaches a composition comprising vitamins, enzymes, coenzymes, minerals, trace elements and/or microorganisms that are embedded, separately with regard to function in carrier substances with formation of protective films against harmful effects so that, with sufficient moisture absorption, **in vivo and in vitro biocatalytic processes can be initiated and controlled** as discussed in the rejection above. Therefore adding the step of active ingredients in a sequential manner will be a repetitive process. Instant invention provides that no antagonistic interaction exists between two active ingredients which is also obvious over the teachings of prior art because Walter teaches embedding various active separately with regard to function. While it is true that Walter does not exemplify the sequential

incorporation of active ingredients, however repetition of step will be obvious over the teachings of prior art.

Applicant argues that in figures 2-4 and in example 3, applicant claims a method of treating a patient using a matrix in which active ingredients have been added sequentially to the matrix in order to create a granular matrix composition that simultaneously separates active agents from one another and serves to slow their absorption in the digestive tract of a patient. The Applicant's invention lies in part in recognizing that if active agents are sequentially added to a granular polysaccharide matrix the ingredients will segregate separately from one another thereby creating a final polysaccharide matrix which separates the ingredients from one another. In contrast, Walter teaches mixing active before adding them to a matrix. See Walters, Examples 1-8, pages 6-10. Applicant respectfully submits that the additional steps taught by the applicants serve to demonstrate that the granular matrix created by the application is not obvious over the compounds recited in the prior art as a matrix made using these steps is neither disclosed nor made obvious by a combination of Shibata and Walter.

Applicants arguments are not persuasive, first instant claims are not directed to method of treating a patient rather the claims are directed to method of providing a human or animal with at least two active substances.. additionally, as stated above since Walter teaches mixing active with galactomannan, one of ordinary would envisage duplicating such application in order to provide benefit of two different actives to human or animal with an expectation to have no interaction between the two actives once

administered because incorporating within galactomannan will prevent interaction from other active due to the envelope created by galactomannan, based on the fact discussed in the reference of Walter which teaches that vitamins, enzymes, coenzymes, minerals, trace elements and/or microorganisms are embedded, **separately with regard to function in carrier substances** with formation of **protective films** against harmful effects so that, with sufficient moisture absorption, **in vivo and in vitro biocatalytic processes can be initiated and controlled.**

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/

Examiner, Art Unit 1612

/Gollamudi S Kishore/

Primary Examiner, Art Unit 1612